Palladium-Catalyzed Alkynylation (Sonogashira Coupling) at C-5 of the Uracil Moiety in Modified Unsaturated Pyranosyl Nucleosides

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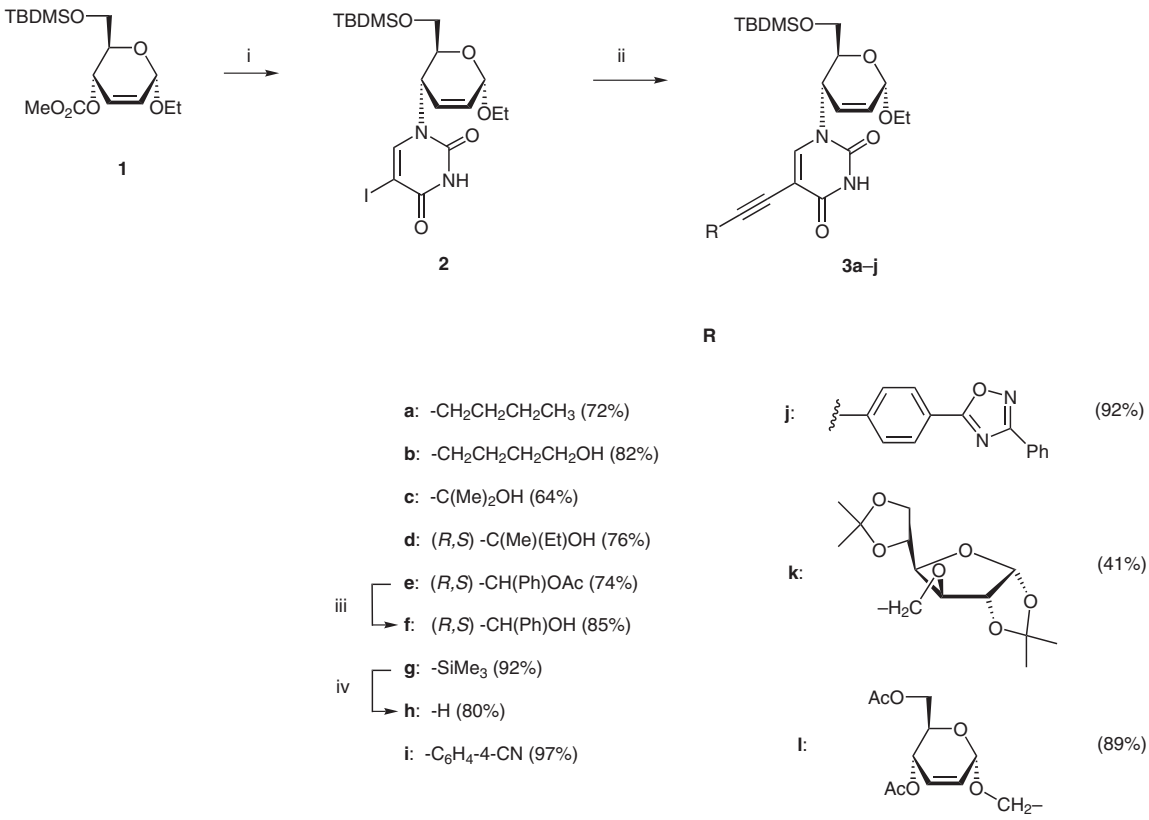
Abstract: Various unsaturated 4-(5-substituted-uracil-1-yl)glycopyranosides were synthesized in good yields by a palladium-catalyzed cross-coupling reaction of ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-4-[5-iodo-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside with a range of acetylenic derivatives.

Key words: palladium, unsaturated carbohydrates, cross-coupling, nucleoside



Scheme 1 *Reagents and conditions*: (i) 5-iodouracil, $Pd(Ph_3P)_4$ (5 mol%), dppb (10 mol%), THF, 60 °C, 45%; (ii) RC≡CH, $Pd(OAc)_2$ (10 mol%), Ph_3P (30 mol%), CuI, DMF, Et_3N, r.t., 2 h; (iii) K_2CO_3, MeOH, H_2O, r.t., 18 h; (iv) MeONa, MeOH, r.t., 1 h.

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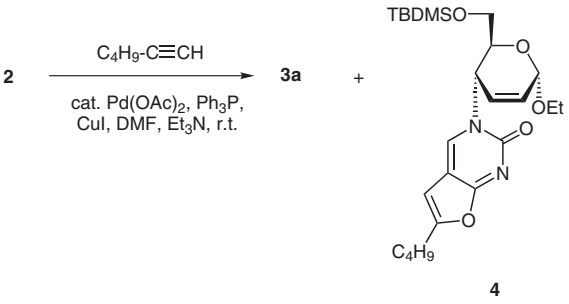
During the last three decades, there has been an increasing interest in the chemistry of nucleosides and modified nucleosides, since nucleosides analogues are active antiviral drugs.[1] Unsaturated analogues of nucleosides are of current interest, since they have been shown to be highly effective as antiviral and antitumor agents.[2] Although significant attention has been paid to the development of synthetic methods for five-membered-ring structures,[3] few examples have been published on the corresponding unsaturated pyranosyl[4] or cyclohexenyl[5] analogues.

We have recently shown that the palladium-catalyzed alkylation of 2,3-unsaturated carbohydrates with heterocyclic amines, such as 5-halogenouracil, allowed an easy access to unsaturated glycopyranosyl nucleosides.[6] The Sonogashira reaction has been shown to be a robust and versatile C–C coupling reaction, and has been used successfully in nucleoside and nucleobase chemistry,[7] allowing an easy access to various C-5 substituted nucleosides. We present in this paper the application of this methodology for the introduction of acetylenic substituents at C-5 of the uracil portion in modified nucleosides.

The key carbohydrate precursor was 4-(5-iodouracil-1-yl) derivative **2** prepared from unsaturated carbohydrate **1** by palladium-catalyzed alkylation with 5-iodouracil as previously described.[6] Treatment of compound **2** with hex-1-yne for two hours in DMF/Et_3N at room temperature in the presence of a catalytic amount of $Pd(OAc)_2/Ph_3P$ and CuI gave coupling product **3a** in 72% yield (Scheme 1), together with a small amount of 3-glycosyl-6-butylfurano[2,3-*d*]pyrimidin-2-one (**4**, 5% yield) (Scheme 2). Keeping the reaction mixture at room temperature for five days gave compounds **3a** and **4** in 62% and 29% yield, respectively. The formation of such furanopyrimidine byproducts has already been described in the literature.[1e,8] Increasing the reaction temperature provides such cyclized products in almost quantitative yields.

Analogous coupling of compound **2** with hex-5-yn-1-ol and 2-methylbut-3-yn-2-ol gave the expected compounds **3b** and **3c** in 82 and 64% yields, respectively. Racemic 3-methylpent-1-yn-3-ol and 1-phenylprop-2-ynyl acetate underwent catalytic coupling with compound **2** to give **3d** and **3e** in 76% and 74% yield, respectively. Compounds **3d** and **3e** are obtained as a 1:1 mixture of the two epimers as shown by ^1H NMR spectroscopy; compound **3d** shows two signals for $CH_3CH_2C(OH)$ at δ = 1.72 and 1.73, and compound **3e** two different signals for H-3 (δ = 5.73 and 5.75), =CHN (δ = 7.51 and 7.61), and NH (δ = 8.15 and 8.20). The same 1:1 ratio was obtained when the reaction was performed in the presence of a large excess of racemic acetylenic alcohol or acetate, showing that no kinetic resolution occurred in this case.

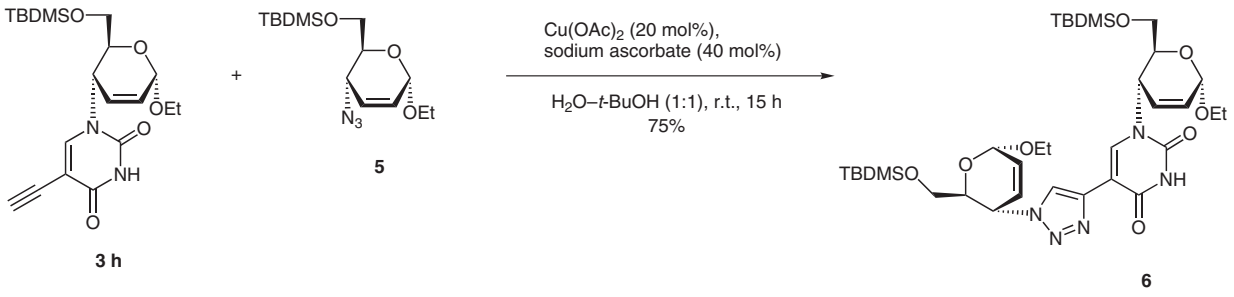


Scheme 2

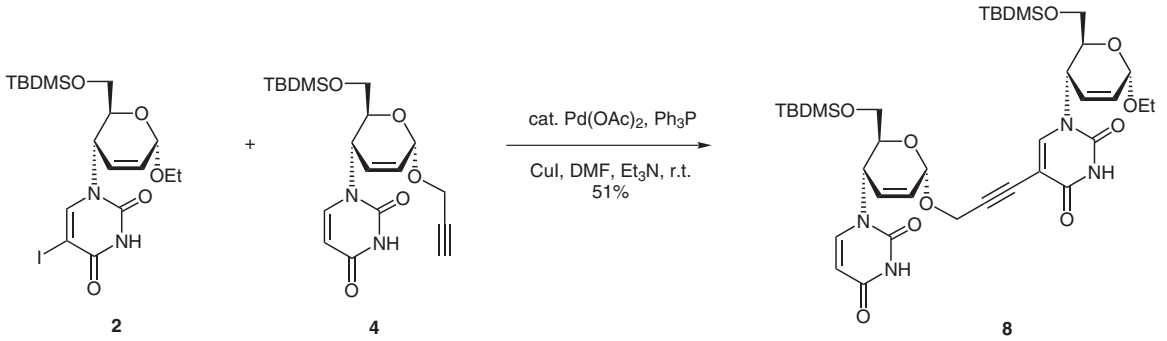
5-Ethynyluracil[9] underwent palladium-catalyzed coupling with carbohydrate **2**, giving compound **3g** in 92% yield. The trimethylsilyl group was easily removed using NaOMe in methanol affording uracil derivative **3h** bearing a terminal acetylenic group in 80% yield. This compound **3h** could be the precursor of a large variety of glycoconjugates using the copper-catalyzed condensation with azidocarbohydrates, the so-called 'click' chemistry.[10] Copper(I)-catalyzed condensation of **3h** with unsaturated azidocarbohydrate **5**[11] afforded effectively 1,2,3-triazole linked disaccharide **6** in 75% yield (Scheme 3).

4-Ethynylbenzonitrile and 5-(4-ethynylphenyl)-3-phenyl-1,2,4-oxadiazole reacted also with compound **2** in the presence of palladium catalyst to give the corresponding coupling products **3i** and **3j** in 97% and 92% yield, respectively. The last coupling allows the easy introduction of the 1,2,4-oxadiazole moiety, exhibiting generally a wide range of biological activities, on the unsaturated 4-(uracil-1-yl)glycopyranoside.

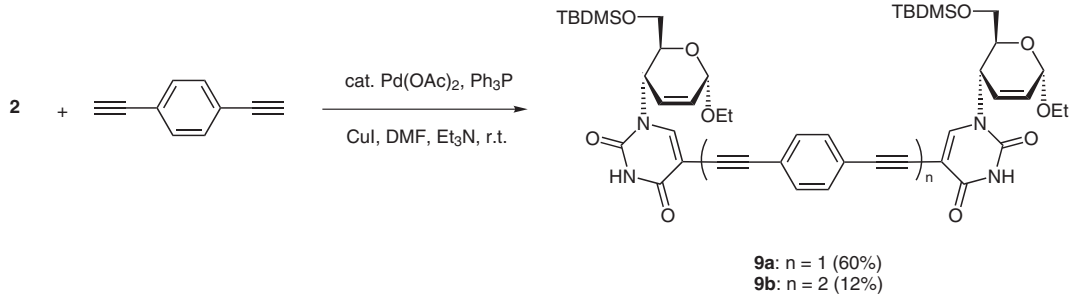
We extended this palladium-catalyzed coupling reaction to more complex propargylic substrates. Condensation of compound **2** with 1,2;5,6-bis-*O*-isopropylidene-3-*O*-(prop-2-yn-1-yl)-α-D-glucofuranose[12] and prop-2-yn-1-yl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[13] afforded disaccharides **3k** and **3l**, bearing two different carbohydrate units on the uracil framework, in 41% and 89% yields, respectively.



Scheme 3



Scheme 4



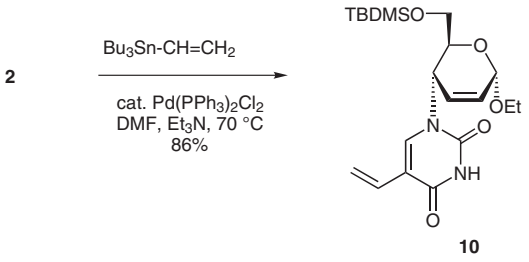
Scheme 5

Cross-coupling of iodo derivative **2** with the ethynylated nucleoside **7**, obtained by a palladium(0)-catalyzed alkylation of carbonate of propynyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside with uracil using a methodology described previously by our group,[6] gave disaccharide **8**, bearing two uracil as well as two unsaturated carbohydrate moieties linked by an acetylenic bond, in 51% chemical yield (Scheme 4).

This coupling reaction was extended also to multivalent alkynes, in order to investigate the potentiality of this methodology for the preparation of polyvalent glycoconjugate clusters. Palladium-catalyzed coupling of carbohydrate **2** in excess with 1,4-diethynylbenzene afforded disaccharide **9a** in 60% yield, together with compound **9b**, in 12% yield (Scheme 5). The later compound was probably formed by the homocoupling of the acetylenic intermediate obtained from the monoalkynylation of diethynylbenzene.

It is to be noticed that compound **2** is a very important precursor for use not only in Sonogashira coupling, but also in other palladium-catalyzed carbon–carbon coupling reaction. For example, palladium-catalyzed coupling of unsaturated 4-(5-iodouracil-1-yl)glycoside **2** with tributylvinyltin at 70 °C in DMF–Et_3N afforded the coupling product **10** in 86% yield (Scheme 6).

In conclusion the palladium-catalyzed Sonogashira coupling between ethyl 4-(5-iodouracil-1-yl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-pyranoside and different functionalized alkynes afforded in good yields a large variety of new unsaturated pyranosyl nucleosides.



Scheme 6

Solvents were dried and distilled by standard methods before use. Most reagents were of commercial quality and used without further purification. Air- and moisture-sensitive reactions were performed under inert atmosphere.

All reactions were monitored by TLC analysis (TLC plates GF_{254} Merck). Column chromatography was performed on silica gel 60 (230–240 mesh, Merck). Optical rotations were recorded using a PerkinElmer 241 polarimeter. Melting points were obtained using a Büchi apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, on a Bruker AMX 300 spectrometer. Chemical shifts (δ) are reported in ppm downfield from TMS or from residual solvent peak; coupling constants (*J*) are reported in Hz and refer to apparent peak multiplicity. Exact mass measurements of the molecular ions were obtained on a Finnigan Mat 95 XL spectrometer.

Ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-4-[5-iodo-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-α-D-*erythro*-hex-2-enopyranoside (**2**),[6] 5-[2-(trimethylsilyl)ethynyl]uracil,[9] (prop-2-yn-1-yl) 2,3-dideoxy-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-2-enopyranoside (**7**),[14] 1,2;5,6-bis-*O*-isopropylidene-3-*O*-(prop-2-yn-1-yl)-α-D-glucofuranose,[12] prop-2-yn-1-yl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside,[13] and ethyl 4-azido-6-

O-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-pyranoside (**5**)[11] were prepared according to reported procedures. Hexanes used had bp 40–65 °C.

5-(4-Ethynylphenyl)-3-phenyl-1,2,4-oxadiazole

To a solution of benzamidoxime (0.5 g, 3.47 mmol) in anhyd CH_2Cl_2 was added at r.t. and under N_2, 4-ethynylbenzoic acid (1.01 g, 6.94 mmol) and DCC (1.43 g, 6.94 mmol). After stirring for 3 h, the solid was filtered off, the solvent was evaporated under reduced pressure, and the residue was submitted to the thermal cyclization reaction at 110–120 °C for 4 h. The resulting mixture was submitted to column chromatography on silica gel (hexanes–EtOAc, 7:3) to give 5-(4-ethynylphenyl)-3-phenyl-1,2,4-oxadiazole (461 mg, 54%) as a colorless solid; mp 99–100 °C; R_f = 0.6 (hexanes–EtOAc, 7:3).

^{1}H NMR ($CDCl_3$): δ = 3.21 (s, 1 H, C≡CH), 7.51–7.63 (m, 5 H_{arom}), 8.13 (br d, J = 6.7 Hz, 2 H_{arom}), 8.21 (br d, J = 6.7 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 79.7, 83.5, 124.5, 125.3, 127.5, 127.8, 128.6, 129.5, 133.0, 133.2, 168.7, 176.3.

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{10}N_2O$: 246.0793; found: 246.0805.

Prop-2-yn-1-yl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3-dideoxy-4-*O*-(methoxycarbonyl)-α-D-*erythro*-hex-2-enopyranoside

To a solution of prop-2-yn-1-yl 2,3-dideoxy-6-*O*-(*tert*-butyldimethylsilyl)-α-D-*erythro*-hex-2-enopyranoside (3.77 g, 12.64 mmol) in CH_2Cl_2 (50 mL) maintained at 0 °C was added pyridine (2.15 mL, 25.1 mmol), 4-dimethylaminopyridine (800 mg, 6.55 mmol), and methyl chloroformate (1.95 mL, 25.1 mmol). After stirring at r.t. for 20 h, H_2O (5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). Evaporation of the solvent under reduced pressure followed by column chromatography on silica gel (hexanes–EtOAc, 5:1) gave the corresponding carbonate (3.3 g, 73%) as a colorless oil; R_f = 0.63; $[\alpha]_D^{25}$ +144.5 (c = 1.1, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.82 (s, 9 H, t-C_4H_9), 2.36 (t, J = 2.4 Hz, 1 H, C≡CH), 3.69 (dd, J = 11.2, 4.7 Hz, 1 H, H-6), 3.72 (s, 3 H, OCH_3), 3.74 (dd, J = 11.2, 2.6 Hz, 1 H, H-6), 3.86 (ddd, J = 9.4, 4.7, 2.6 Hz, 1 H, H-5), 4.24 (d, J = 2.4 Hz, 2 H, CH_2C≡), 5.11 (br d, J = 9.4 Hz, 1 H, H-4), 5.15 (br s, 1 H, H-1), 5.76 (ddd, J = 10.1, 2.6, 2.4 Hz, 1 H, H-3), 5.92 (br d, J = 10.1 Hz, 1 H, H-2).

^{13}C NMR ($CDCl_3$): δ = –5.1, 18.7, 26.2, 55.0, 55.2, 62.7, 69.2, 69.7, 75.1, 79.5, 92.7, 127.9, 129.8, 155.4.

Anal. Calcd for $C_{17}H_{28}O_6Si$: C, 57.28; H, 7.92. Found: C, 57.04; H, 8.03.

Prop-2-yn-1-yl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (7)

To a solution of $Pd(Ph_3P)_4$ (31 mg, 34 μmol), dppb (58 mg, 136 μmol), and the unsaturated carbohydrate (500 mg, 1.4 mmol) in THF (5 mL) was added uracil (235 mg, 2.1 mmol) in THF (2 mL). The solution was stirred at 50 °C for 4 h. Evaporation of the solvent under reduced pressure gave a residue that was directly purified by column chromatography on silica gel (hexanes–EtOAc, 4:1) to give carbohydrate **7** (350 mg, 42%) as a colorless solid; mp 158–159 °C; R_f = 0.28 (hexanes–EtOAc, 4:1); $[\alpha]_D^{25}$ +31.5 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.87 (s, 9 H, t-C_4H_9), 2.47 (t, J = 2.3 Hz, 1 H, C≡CH), 3.69 (dd, J = 11.3, 5.4 Hz, 1 H, H-6), 3.73 (dd, J = 11.3, 4.3 Hz, 1 H, H-6), 3.83–3.88 (m, 1 H, H-5), 4.33 (d, J = 2.3 Hz, 2 H, CH_2C≡C), 5.21 (br d, J = 9.7 Hz, 1 H, H-4), 5.28 (br s, 1 H, H-1), 5.73 (d, J = 8.1 Hz, 1 H, =CHCO), 5.78 (br d, J = 10.0 Hz, 1 H, H-3), 6.09 (ddd, J = 10.0, 2.8, 2.6 Hz, 1 H, H-2), 7.21 (d, J = 8.1 Hz, 1 H, =CHN), 8.09 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 18.7, 26.2, 51.0, 55.2, 63.9, 71.5, 75.4, 79.3, 92.2, 103.4, 129.6, 130.5, 141.5, 151.7, 163.9.

Anal. Calcd for $C_{19}H_{28}N_2O_5Si$: C, 58.14; H, 7.19. Found: C, 57.92; H, 7.31.

Palladium-Catalyzed Preparation of Compounds 3a–e,g,i–l; General Procedure

A solution of $Pd(OAc)_2$ (6.8 mg, 0.03 mmol) and Ph_3P (23.4 mg, 0.09 mmol) in DMF (2 mL) was stirred at r.t. in a Schlenk tube under argon for 15 min. This solution was added to a mixture of the carbohydrate derivative **2** (0.3 mmol), CuI (11.4 mg, 0.06 mmol), and Et_3N (1.21 mL, 9 mmol), in DMF (1 mL), followed by the addition of the alkyne (0.9 mmol). After stirring for 2 hours at r.t., the solution was filtered through Celite, and the solid was washed with EtOAc (2 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel using the indicated solvents.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-hex-1-yn-1-yl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3a)

Prepared from **2** and hex-1-yne; colorless solid; yield: 100 mg (72%); mp 43–46 °C; R_f = 0.77 (CH_2Cl_2–EtOAc, 7:3); $[\alpha]_D^{25}$ +87.7 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.83 (s, 9 H, t-C_4H_9), 0.93 (t, J = 7.1 Hz, 3 H, CH_3), 1.27 (t, J = 7.1 Hz, 3 H, C$H_3$$CH_2$O), 1.41 (sext, J = 6.8 Hz, 2 H, CH_2), 1.54 (quint, J = 6.8 Hz, 2 H, CH_2), 2.40 (t, J = 7.1 Hz, 2 H, CH_2), 3.60 (dq, J = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.68–3.72 (m, 2 H, H-6), 3.84–3.94 (m, 2 H, CH_3CH_2O, H-5), 5.07 (br s, 1 H, H-1), 5.20 (br d, J = 8.5 Hz, 1 H, H-4), 5.76 (br d, J = 10.1 Hz, 1 H, H-3), 6.09 (ddd, J = 10.1, 2.6, 2.6 Hz, 1 H, H-2), 7.37 (s, 1 H, =CHN), 9.22 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 14.0, 15.6, 18.7, 19.7, 22.4, 26.2, 30.9, 51.5, 64.1, 64.6, 71.1, 77.6, 93.9, 96.1, 101.8, 128.9, 131.3, 143.2, 150.6, 162.1.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{38}N_2O_5Si$ + Na: 485.2448; found: 485.2446.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-4-[6-butyl-2-oxofuro[2,3-*d*]pyrimidin-3(2*H*)-yl]-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (4)

Obtained from **2** and hex-1-yne; yellow solid; yield: 7 mg (5%); mp 91.5–94 °C; R_f = 0.53 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{25}$ –16 (c = 1.3, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.81 (s, 9 H, t-C_4H_9), 0.94 (t, 3 H, J = 7.3 Hz, CH_3), 1.27 (t, J = 7.0 Hz, 3 H, C$H_3$$CH_2$O), 1.40 (sext, J = 7.3 Hz, 2 H, CH_2), 1.67 (quint, J = 7.5 Hz, 2 H, CH_2), 2.64 (t, J = 7.3 Hz, 2 H, CH_2), 3.60 (dq, J = 9.6, 7.0 Hz, 1 H, CH_3CH_2O), 3.73 (dd, J = 11.5, 7.4 Hz, 1 H, H-6), 3.76 (dd, J = 11.5, 6.3 Hz, 1 H, H-6), 3.88–3.98 (m, 2 H, CH_3CH_2O, H-5), 5.13 (br s, 1 H, H-1), 5.61 (br d, J = 8.2 Hz, 1 H, H-4), 5.77 (dd, J = 9.9, 1.5 Hz, 1 H, H-3), 6.06 (s, 1 H, = CH-), 6.12 (ddd, J = 9.9, 2.6, 2.6 Hz, 1 H, H-2), 7.80 (s, 1 H, CHN).

^{13}C NMR ($CDCl_3$): δ = –5.1. –5.0. 14.1, 15.6, 18.6, 22.5, 26.2, 28.4, 29.2, 52.7, 63.9, 64.5, 73.7, 93.8, 98.8, 108.9, 129.6, 151.1, 156.0, 160.9, 162.7.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{38}N_2O_5Si$ + Na: 485.2448; found: 485.2446.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-(6-hydroxyhex-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3b)

Prepared from **2** and hex-5-yn-1-ol; colorless solid; yield: 115 mg (82%); mp 50–52 °C; R_f = 0.28 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{25}$ +74.4 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.04 (s, 3 H, $SiCH_3$), 0.05 (s, 3 H, $SiCH_3$), 0.88 (s, 9 H, *t*-C_4H_9), 1.28 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 1.69–1.75 (m, 5 H, CH_2, OH), 2.46 (t, *J* = 6.5 Hz, 2 H, $CH_2C{\equiv}$), 3.60 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.66–3.74 (m, 4 H, H-6, C*H*$_2$OH), 3.85–3.96 (m, 2 H, CH_3CH_2O, H-5), 5.09 (br s, 1 H, H-1), 5.23 (br d, *J* = 8.1 Hz, 1 H, H-4), 5.76 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.10 (ddd, *J* = 10.1, 2.6, 2.6 Hz, 1 H, H-2), 7.42 (s, 1 H, =CHN), 8.85 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 19.7, 25.0, 26.2, 32.2, 51.5, 62.5, 64.1, 64.7, 71.2, 71.6, 93.9, 96.0, 101.7, 128.9, 131.3, 143.3, 150.6, 162.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{38}N_2O_6Si$ + Na: 501.2397; found: 501.2397.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-(3-hydroxy-3-methylbut-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3c)

Prepared from **2** and 2-methylbut-3-yn-2-ol; yellow solid; yield: 90 mg (64%); mp 66–68 °C; R_f = 0.38 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{25}$ +83.2 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.05 (s, 3 H, $SiCH_3$), 0.06 (s, 3 H, $SiCH_3$), 0.88 (s, 9 H, *t*-C_4H_9), 1.29 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 2.88 (br s, 1 H, OH), 3.62 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.70 (dd, *J* = 11.1, 4.1 Hz, 1 H, H-6), 3.75 (dd, *J* = 11.1, 4.1 Hz, 1 H, H-6), 3.86–3.96 (m, 2 H, CH_3CH_2O, H–5), 5.10 (br s, 1 H, H-1), 5.23 (br d, *J* = 5.4 Hz, 1 H, H-4), 5.77 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.12 (ddd, *J* = 10.1, 2.4, 2.2 Hz, 1 H, H-2), 7.46 (s, 1 H, =CHN), 8.76 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$) δ = –5.1, –5.0, 15.6, 18.7, 26.2, 31.5, 31.6, 51.2, 64.0, 64.7, 65.6, 71.4, 72.9, 93.9, 99.8, 100.8, 128.8, 131.4, 143.8, 150.5, 162.1.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{36}N_2O_6Si$ + Na: 487.2240; found: 487.2240.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-(*R*,*S*)-3-hydroxy-3-methylpent-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3d)

Prepared from **2** and 3-methylpent-1-yn-3-ol; colorless solid; yield: 109 mg (76%); mp 56–60 °C; R_f = 0.47 (CH_2Cl_2–EtOAc, 1:1).

^{1}H NMR ($CDCl_3$): δ = –0.01 [s, 6 H, $Si(CH_3)_2$], 0.82 (s, 9 H, *t*-C_4H_9), 1.03 (t, *J* = 7.4 Hz, 3 H, C*H*$_3$CH$_2$), 1.23 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 1.50 (s, 3 H, CH_3), 1.72 and 1.73 [2 q, *J* = 7.4 Hz, 2 H, CH_3CH_2C, *R* and *S*], 2.58 (br s, 1 H, OH), 3.56 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.65 (dd, *J* = 11.3, 5.5 Hz, 1 H, H-6), 3.69 (dd, *J* = 11.3, 4.3 Hz, 1 H, H-6), 3.80–3.91 (m, 2 H, CH_3CH_2O, H-5), 5.04 (br s, 1 H, H-1), 5.18 (br d, *J* = 7.3 Hz, 1 H, H-4), 5.71 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.06 (ddd, *J* = 10.1, 2.4, 2.4 Hz, 1 H, H-2), 7.40 (s, 1 H, =CHN), 8.60 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 9.4, 15.5, 18.7, 26.2, 29.36, 29.2, 29.3, 36.7, 36.8, 51.5, 64.0, 64.6, 69.2, 71.3, 74.0, 93.9, 98.7, 100.9, 128.7, 131.3, 143.5, 150.6, 162.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{38}N_2O_6Si$ + Na: 501.2397; found: 501.2395.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-(*R*,*S*)-3-acetoxy-3-phenylprop-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3e)

Prepared from **2** and 1-phenylprop-2-ynyl acetate; brown solid; yield: 122 mg (74%); mp 62–65 °C; R_f = 0.46 (CH_2Cl_2–EtOAc, 4:1).

^{1}H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 (s, 9 H, *t*-C_4H_9), 1.27 and 1.28 [2 t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O, *R* and *S*], 1.50 (s, 3 H, CH_3), 2.12 (s, 3 H, CH_3CO), 3.54–3.64 (m, 1 H, CH_3CH_2O), 3.65–3.76 (m, 2 H, H-6), 3.83–3.94 (m, 2 H, CH_3CH_2O, H-5), 5.07 (br s, 1 H, H-1), 5.21 (br d, *J* = 7.3 Hz, 1 H, H-4), 5.73 and 5.75 [2 br d, *J* = 10.0 Hz, 1 H, H-3, *R* and *S*], 6.10 (ddd, *J* = 10.0, 2.6, 2.6 Hz, 1 H, H-2), 6.66 (s, 1 H, CHC≡C), 7.35–7.43 (m, 3 H_{arom}), 7.51 and 7.61 [2 s, 1 H, = CHN, *R* and *S*], 7.58 (dd, *J* = 7.9, 2.1 Hz, 2 H_{arom}), 8.15 and 8.20 [2 br s, 1 H, NH, *R* and *S*].

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 21.5, 26.2, 51.7, 64.1, 64.3, 64.7, 66.3, 69.2, 71.2, 78.2, 91.0, 93.9, 100.1, 128.3, 128.6, 128.8, 129.1, 129.4, 131.5, 136.9, 144.9, 150.6, 151.4, 160.5, 161.7, 170.2.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{38}N_2O_7Si$ + Na: 577.2346; found: 577.2348.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[2,4-dioxo-5-(trimethylsilylethynyl)-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3g)

Prepared from **2** and ethynyltrimethylsilane; yellow solid; yield: 131.5 mg (92%); mp 68–71 °C; R_f = 0.72 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{25}$ +106.5 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 (s, 3 H, $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.24 (s, 9 H, *t*-C_4H_9), 0.87 (s, 9 H, *t*-C_4H_9), 1.28 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 3.62 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.66 (dd, *J* = 11.1, 5.2 Hz, 1 H, H-6), 3.71 (dd, *J* = 11.1, 4.7 Hz, 1 H, H-6), 3.84–3.95 (m, 2 H, CH_3CH_2O, H-5), 5.08 (br s, 1 H, H-1), 5.22 (br d, *J* = 8.7 Hz, 1 H, H-4), 5.76 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.10 (ddd, *J* = 10.1, 2.4, 2.4 Hz, 1 H, H-2), 7.50 (s, 1 H, =CHN), 8.09 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.3, –5.2, 15.4, 18.5, 26.0, 51.3, 63.8, 64.5, 71.0, 93.7, 94.9, 100.2, 101.0, 128.6, 131.0, 144.7, 150.3, 161.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{38}N_2O_5Si$ + Na: 501.2217; found: 501.2218.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[2,4-dioxo-5-(4-cyanophenylethynyl)-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3i)

Prepared from **2** and 4-ethynylbenzonitrile; yellow solid; yield: 147 mg (97%); mp 137–139 °C; R_f = 0.52 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{25}$ +148.9 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = –0.01 (s, 3 H, $SiCH_3$), 0.00 (s, 3 H, $SiCH_3$), 0.82 (s, 9 H, *t*-C_4H_9), 1.24 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 3.57 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.66 (dd, *J* = 11.1, 5.6 Hz, 1 H, H-6), 3.71 (dd, *J* = 11.1, 4.5 Hz, 1 H, H-6), 3.81–3.91 (m, 2 H, CH_3CH_2O, H-5), 5.05 (br s, 1 H, H-1), 5.24 (br d, *J* = 7.9 Hz, 1 H, H-4), 5.74 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.09 (ddd, *J* = 10.1, 2.4, 2.4 Hz, 1 H, H-2), 7.54–7.60 (m, 5 H, 4 H_{arom}, =CHN), 8.82 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 26.2, 52.0, 64.3, 64.8, 71.3, 84.8, 92.8, 94.0, 100.4, 112.1, 118.8, 127.8, 128.7, 131.6, 132.4, 132.5, 144.8, 150.5, 161.5.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{33}N_3O_5Si$ + Na: 530.2087; found: 530.2084.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[2,4-dioxo-5-{[4-(3-phenyl-1,2,4-oxadiazol-5-yl)phenyl]ethynyl}-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3j)

Prepared from **2** and 5-(4-ethynylphenyl)-3-phenyl-1,2,4-oxadiazole; yellow solid; yield: 172 mg (92%); mp 84–86 °C; R_f = 0.45 (CH_2Cl_2–EtOAc, 9:1); $[\alpha]_D^{25}$ +124.2 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.05 [s, 6 H, $Si(CH_3)_2$], 0.88 (s, 9 H, *t*-C_4H_9), 1.29 (t, *J* = 7.1 Hz, 3 H, C*H*$_3$CH$_2$O), 3.62 (dq, *J* = 9.7, 7.1 Hz, 1 H, CH_3CH_2O), 3.71 (dd, *J* = 11.1, 5.3 Hz, 1 H, H-6), 3.76 (dd, *J* = 11.1, 4.7 Hz, 1 H, H-6), 3.86–3.96 (m, 2 H, CH_3CH_2O, H-5), 5.10 (br s, 1 H, H-1), 5.28 (br d, *J* = 7.9 Hz, 1 H, H-4), 5.80 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.14 (ddd, *J* = 10.1, 2.4, 2.8 Hz, 1 H, H-2), 7.53–7.64 (m,

4 H, 3 H_{arom}, =CHN), 7.67 (d, J = 8.5 Hz, 2 H_{arom}), 8.05 (br s, 1 H, NH), 8.17 (d, J = 8.5 Hz, 2 H_{arom}), 8.22 (dd, J = 8.3 Hz, 2 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = –5.08, –5.02, 15.6, 18.8, 26.2, 53.8, 64.3, 64.8, 71.3, 82.4, 94.0, 94.1, 101.0, 124.6, 125.8, 127.2, 1278, 128.6, 128.8, 129.5, 132.5, 133.2, 145.9, 150.5, 161.4, 168.8, 176.2.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{34}H_{38}N_4O_6Si$ + Na: 649.2458; found: 649.2454.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-4-[5-{3-(2,3;5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yl)prop-1-yn-1-yl}-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (3k)

Prepared from **2** and 1,2;5,6-di-*O*-isopropylidene-3-*O*-propargyl-α-D-glucofuranose; colorless solid; yield: 83.5 mg (41%); mp 69–71 °C; R_f = 0.31 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{25}$ +55.7 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 (s, 9 H, t-C_4H_9), 1.27 (t, J = 7.0 Hz, 3 H, CH_3CH_2O), 1.32 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 3.60 (dq, J = 9.6, 7.0 Hz, 1 H, CH_3CH_2O), 3.68 (dd, J = 11.1, 5.6 Hz, 1 H, H-6), 3.73 (dd, J = 11.1, 4.5 Hz, 1 H, H-6), 3.83–3.93 (m, 2 H, CH_3CH_2O, H-5), 4.00 (dd, J = 8.5, 5.3 Hz, 1 H, H-4′), 4.08–4.15 (m, 3 H, H-6′, H-5′), 4.26–4.33 (m, 1 H, H-3′), 4.45 (d, J = 15.8 Hz, 1 H, CH_2C≡), 4.52 (d, J = 15.8 Hz, 1 H, CH_2C≡), 4.70 (d, J = 3.7 Hz, 1 H, H-2′), 5.08 (br s, 1 H, H-1), 5.24 (br d, J = 8.8 Hz, 1 H, H-4), 5.74 (br d, J = 10.0 Hz, 1 H, H-3), 5.88 (d, J = 3.7 Hz, 1 H, H-1′), 6.11 (ddd, J = 10.0, 2.8, 2.6 Hz, 1 H, H-2), 7.50 (s, 1 H, = CHN), 8.02 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 25.8, 26.2, 26.2, 27.2, 27.3, 51.8, 59.2, 64.2, 64.7, 67.6, 71.2, 72.8, 77.4, 81.5, 82.2, 83.1, 90.3, 93.9, 100.3, 105.6, 109.4, 112.2, 128.6, 131.6, 145.0, 150.5, 161.6.

Anal. Calcd for $C_{33}H_{50}N_2O_{11}Si$: C, 58.39; H, 7.42. Found: C, 58.06; H, 7.48.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-{3-[(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)oxy]-prop-1-yn-1-yl}-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3l)

Prepared from **2** and prop-2-yn-1-yl-4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranose; yellow solid; yield: 173 mg (89%); mp 52–55 °C; R_f = 0.45 (CH_2Cl_2–EtOAc, 7:3); $[\alpha]_D^{25}$ +146.9 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 (s, 9 H, t-C_4H_9), 1.27 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 2.08 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3), 3.60 (dq, J = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.69–3.71 (m, 2 H, H-6), 3.83–3.93 (m, 2 H, CH_3CH_2O, H-5), 4.08–4.14 (m, 1 H, H-5′), 4.19 (dd, J = 12.0, 2.6 Hz, 1 H, H-6′), 4.25 (dd, J = 12.0, 5.1 Hz, 1 H, H-6′), 4.48 (d, J = 15.8 Hz, 1 H, CH_2C≡), 4.55 (d, J = 15.8 Hz, 1 H, CH_2C≡), 5.07 (br s, 1 H, H-1), 5.24 (br d, J = 10.0 Hz, 1 H, H-4), 5.26 (br s, 1 H, H-1′), 5.34 (ddd, J = 9.6, 1.5, 1.5 Hz, 1 H, H-4′), 5.74 (br d, J = 10.2 Hz, 1 H, H-3), 5.86 (ddd, J = 10.2, 2.4, 1.6 Hz, 1 H, H-3′), 5.93 (br d, J = 10.2 Hz, 1 H, H-2), 6.11 (ddd, J = 10.2, 2.6, 2.6 Hz, 1 H, H-2′), 7.51 (s, 1 H, =CHN), 8.07 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 21.2, 21.3, 26.2, 51.9, 56.2, 63.2, 64.2, 64.7, 65.6, 67.6, 71.2, 77.5, 89.9, 93.2, 93.9, 100.2, 127.7, 128.5, 130.1, 131.6, 144.9, 150.4, 161.5, 170.6, 171.1.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{34}H_{44}N_2O_{11}Si$ + Na: 671.2612; found: 671.2611.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-(*R,S*)-3-hydroxy-3-phenylprop-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3f)

A mixture of compound **3e** (30 mg, 0.052 μmol), and K_2CO_3 (300 mg, 2.17 mmol) in MeOH (5 mL) and H_2O (2 mL) was stirred at r.t. for 18 h. The solution was concentrated under reduced pressure, and the product was extracted with EtOAc (3 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was submitted to column chromatography on silica gel (CH_2Cl_2–EtOAc, 7:3) to give compound **3f** (23.4 mg, 85%) as a colorless solid; mp 68–70 °C; R_f = 0.29 (CH_2Cl_2–EtOAc, 7:3).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.83 (s, 9 H, t-C_4H_9), 1.22 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 2.87 and 2.94 [2 br s, 1 H, OH, *R* and *S*], 3.55 (dq, J = 9.4, 7.1 Hz, 1 H, CH_3CH_2O), 3.64 (dd, J = 11.3, 5.8 Hz, 1 H, H-6), 3.69 (dd, J = 11.3, 4.5 Hz, 1 H, H-6), 3.79–3.89 (m, 2 H, CH_3CH_2O, H-5), 5.03 (br s, 1 H, H-1), 5.19 (br d, J = 5.4 Hz, 1 H, H-4), 5.67 and 5.69 (2 s, 1 H, C≡CH, *R* and *S*], 5.70 (br d, J = 10.0 Hz, 1 H, H-3), 6.06 (br d, J = 10.0 Hz, 1 H, H-2), 7.27–7.38 (m, 3 H_{arom}), 7.47 (s, 1 H, =CHN), 7.56 (d, J = 7.1 Hz, 2 H_{arom}), 8.56 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.0, 15.6, 18.8, 26.2, 51.7, 64.1, 64.7, 65.2, 71.3, 77.2, 77.6, 93.9, 94.9, 100.4, 127.1, 127.2, 128.6, 128.7, 129.0, 130.5, 140.6, 144.5, 150.4, 162.0.

Anal. Calcd for $C_{27}H_{36}N_2O_6Si$: C, 63.25; H, 7.08. Found: C, 63.08; H, 7.12.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-ethynyl-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (3h)

To a solution of compound **3g** (822 mg, 1.72 mmol) in MeOH (1.5 mL) maintained at 0 °C was added a solution of MeONa (1.5 g, 7.74 mmol) in MeOH (5.3 mL). After stirring for 1 h at r.t., a sat. aq solution of NH_4Cl (5 mL) was added, and the mixture was extracted with EtOAc (3 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified directly purified by column chromatography on silica gel (CH_2Cl_2–EtOAc, 4:1) to give carbohydrate **3h** (562 mg, 80%) as a colorless solid; mp 153–155 °C; R_f = 0.36; $[\alpha]_D^{25}$ +73.4 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.03 [s, 6 H, $Si(CH_3)_2$], 0.86 (s, 9 H, t-C_4H_9), 1.27 (t, J = 7.1 Hz, 3 H, CH_3CH_2O), 3.22 (s, 1 H, HC≡C), 3.60 (dq, J = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.68 (dd, J = 11.1, 5.4 Hz, 1 H, H-6), 3.72 (dd, J = 11.1, 4.7 Hz, 1 H, H-6), 3.83–3.93 (m, 2 H, CH_3CH_2O, H-5), 5.08 (br s, 1 H, H-1), 5.24 (br d, J = 6.8 Hz, 1 H, H-4), 5.75 (br d, J = 10.1 Hz, 1 H, H-3), 6.11 (ddd, J = 10.1, 2.8, 2.6 Hz, 1 H, H-2), 7.52 (s, 1 H, =CHN), 8.26 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.5, 18.7, 26.2, 51.8, 64.2, 64.7, 71.2, 74.7, 82.9, 93.9, 100.0, 128.7, 131.4, 145.3, 150.7, 161.9.

HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{20}H_{30}N_2O_5Si$ + Na: 429.1822; found: 429.1822.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[5-{1-[ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl]-1*H*-1,2,3-triazol-4-yl}-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (6)

Azido sugar **5** (164.5 mg, 0.53 mmol) and alkyne **3h** (405 mg, 1 mmol) were suspended in t-BuOH–H_2O (1:1, 4 mL). To this solution was added a mixture of $Cu(OAc)_2$ (18 mg, 0.10 mmol) and sodium ascorbate (40 mg, 0.2 mmol) in t-BuOH–H_2O (1:1, 1 mL). The mixture was stirred overnight at r.t. under N_2. H_2O (3 mL) was then added, and the product was extracted with CH_2Cl_2 (3 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel (CH_2Cl_2–EtOAc, 4:1) to give compound **6** (286 mg, 75%) as a colorless solid; mp 83–84 °C; R_f = 0.36 (CH_2Cl_2–EtOAc, 4:1); $[\alpha]_D^{25}$ +119.7 (c = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.02 (s, 3 H, $SiCH_3$), 0.03 (s, 6 H, 2 $SiCH_3$), 0.04 (s, 3 H, $SiCH_3$), 0.85 (s, 9 H, *t*-C_4H_9), 0.89 (s, 9 H, *t*-C_4H_9), 1.28 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2), 1.29 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2), 3.57–3.66 (m, 3 H, H-6), 3.69 (br d, *J* = 11.7 Hz, 1 H, H-6), 3.72–3.81 (m, 2 H, CH_2CH_3), 3.87–3.95 (m, 2 H, CH_2CH_3), 4.04 (m, 1 H, H-5′), 4.17 (ddd, J = 9.8, 2.1, 1.6 Hz, 1 H, H-5), 5.10 (br s, 1 H, H-1), 5.16 (br s, 1 H, H-1′), 5.33 (br d, *J* = 5.4 Hz, 1 H, H-4′), 5.40 (br d, *J* = 9.8 Hz, 1 H, H-4), 5.83 (br d, *J* = 10.1 Hz, 1 H, =CH), 5.97 (br d, *J* = 10.1 Hz, 1 H, =CH), 6.05 (ddd, *J* = 10.1, 2.5, 2.5 Hz, 1 H, =CH), 6.11 (br d, *J* = 10.1 Hz, 1 H, =CH), 8.25 (s, 1 H, =CHN), 8.26 (s, 1 H, =CHN), 8.64 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.2, –5.1, –5.0, 15.6, 18.7, 26.2, 55.3, 62.7, 64.3, 64.5, 71.2, 94.1, 94.2, 107.0, 121.5, 128.3, 128.8, 129.4, 139.5, 151.1, 161.4.

Anal. Calcd for $C_{34}H_{57}N_5O_8Si_2$: C, 56.72; H, 7.98. Found: C, 56.78; H, 8.65.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-4-[5-(3-{[6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-4-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-α-D-*erythro*-hex-2-enopyranosid-4-yl]oxy}prop-1-yn-1-yl)-2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl]-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (8)

A solution of $Pd(OAc)_2$ (5.7 mg, 0.025 mmol) and Ph_3P (19.5 mg, 0.075 mmol) in DMF (3 mL) was stirred at r.t. in a Schlenk tube under argon for 15 min. This solution was added to a mixture of the carbohydrate derivative **2** (126.2 mg, 0.25 mmol), CuI (9.5 mg, 0.05 mmol), and Et_3N (1.0 mL, 7.4 mmol), in DMF (1 mL), followed by the addition of 1,4-diethynylbenzene (294 mg, 0.75 mmol). After stirring for 2 h at r.t., the solution was filtered through Celite, and the solid was washed with EtOAc (2 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel (CH_2Cl_2–EtOAc, 1:1) to give compound **8** (98.5 mg, 51%) as a colorless solid; mp 103–106 °C; R_f = 0.28 (CH_2Cl_2–EtOAc, 1:1); $[\alpha]_D^{25}$ +70.2 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.03 [s, 6 H, $Si(CH_3)_2$], 0.87 (s, 18 H, *t*-C_4H_9), 1.27 (t, *J* = 7.0 Hz, 3 H, CH_3CH_2O), 3.60 (dq, *J* = 9.6, 7.0 Hz, 1 H, CH_3CH_2O), 3.66–3.75 (m, 4 H, H-6, H-6′), 3.83–3.94 (m, 3 H, CH_3CH_2O, H-5, H-5′), 4.48 (d, *J* = 15.7 Hz, 1 H, $CH_2C{\equiv}$), 4.56 (d, *J* = 15.7 Hz, 1 H, $CH_2C{\equiv}$), 5.08 (br s, 1 H, H-1), 5.23 (br d, *J* = 9.6 Hz, 2 H, H-4, H-4′), 5.31 (br s, 1 H, H-1′), 5.74 (d, *J* = 8.1 Hz, 1 H, =CHCO), 5.74 (br d, *J* = 10.1 Hz, 1 H, H-3′), 5.79 (br d, *J* = 10.1 Hz, 1 H, H-3), 6.11 (ddd, *J* = 10.1, 2.6, 2.4 Hz, 2 H, H-2, H-2′), 7.22 (d, *J* = 8.1 Hz, 1 H, =CHN), 7.51 (s, 1 H, =CHN), 8.10 (br s, 1 H, NH), 8.18 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.2, –5.1, –5.0, –4.9, 15.6, 18.6, 18.7, 26.1, 26.2, 50.9, 51.7, 56.0, 63.9, 64.4, 64.7, 71.4, 77.8, 89.6, 92.3, 93.9, 100.2, 103.4, 128.6, 129.4, 130.6, 131.6, 141.7, 144.7, 150.8, 151.7, 162.0, 164.0.

Anal. Calcd for $C_{37}H_{56}N_4O_{10}Si_2$: C, 57.49; H, 7.30. Found: C, 56.96; H, 7.41.

Palladium-Catalyzed Condensation of Compound 2 with 1,4-Diethynylbenzene

A solution of $Pd(OAc)_2$ (6.8 mg, 0.03 mmol) and Ph_3P (23.4 mg, 0.09 mmol) in DMF (2 mL) was stirred at r.t. in a Schlenk tube under argon for 15 min. This solution was added to a mixture of the carbohydrate derivative **2** (151.5 mg, 0.3 mmol), CuI (11.4 mg, 0.06 mmol), and Et_3N (1.22 mL, 9 mmol), in DMF (1 mL), followed by the addition of 1,4-diethynylbenzene (18.9 mg, 0.15 mmol). After stirring for 2 h at r.t., the solution was filtered through Celite, and the solid was washed with EtOAc (2 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel (CH_2Cl_2–EtOAc, 6:4) to give compound **9a** (80 mg, 60%) and **9b** (27 mg, 12%).

5,5′-[1,4-Phenylenebis(ethyne-2,1-diyl)]bis[1-{4-[ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl]}pyrimidine-2,4(1*H*,3*H*)-dione] (9a)

Yellow solid; mp 116–119 °C; R_f = 0.70 (CH_2Cl_2–EtOAc, 6:4); $[\alpha]_D^{25}$ +194.7 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 12 H, $Si(CH_3)_2$], 0.83 (s, 18 H, *t*-C_4H_9), 1.24 (t, *J* = 7.1 Hz, 6 H, CH_3CH_2O), 3.56 (dq, *J* = 9.4, 7.1 Hz, 2 H, CH_3CH_2O), 3.66 (dd, *J* = 11.1, 5.4 Hz, 2 H, H-6), 3.71 (dd, *J* = 11.1, 5.0 Hz, 2 H, H-6), 3.80–3.90 (m, 4 H, CH_3CH_2O, H-5), 5.05 (br s, 2 H, H-1), 5.22 (br d, *J* = 7.7 Hz, 2 H, H-4), 5.74 (br d, *J* = 9.9 Hz, 2 H, H-3), 6.08 (ddd, *J* = 9.9, 2.4, 2.4 Hz, 2 H, H-2), 7.45 (s, 4 H_{arom}), 7.52 (s, 2 H, =CHN), 8.21 (br s, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.2, –5.1, 15.6, 18.7, 26.2, 51.5, 64.5, 71.2, 85.2, 93.3, 94.6, 100.6, 123.5, 129.0, 129.2, 131.9, 132.4, 132.6, 145.0, 151.6, 162.6.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{43}H_{62}N_4O_{10}Si_2$ + Na: 909.3902; found: 909.3901.

5,5′-[Buta-1,3-diyne-1,4-diylbis(4,1-phenyleneprop-1-yne-3,1-diyl)]bis[1-{4-[ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl]}pyrimidine-2,4(1*H*,3*H*)-dione] (9b)

Yellow solid; mp 113–116 °C; R_f = 0.81 (CH_2Cl_2–EtOAc, 6:4); $[\alpha]_D^{25}$ +202.5 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.04 [s, 12 H, $Si(CH_3)_2$], 0.86 (s, 18 H, *t*-C_4H_9), 1.28 (t, *J* = 7.1 Hz, 6 H, CH_3CH_2O), 3.56 (dq, *J* = 9.6, 7.1Hz, 2 H, CH_3CH_2O), 3.70 (dd, *J* = 11.1, 5.4 Hz, 2 H, H-6), 3.75 (dd, *J* = 11.1, 4.5 Hz, 2 H, H-6), 3.85–3.95 (m, 4 H, CH_3CH_2O, H-5), 5.09 (br s, 2 H, H-1), 5.22 (br d, *J* = 9.9 Hz, 2 H, H-4), 5.78 (br d, *J* = 10.1 Hz, 2 H, H-3), 6.13 (ddd, *J* = 10.1, 2.4, 2.4 Hz, 2 H, H-2), 7.49 (s, 8 H_{arom}), 7.57 (s, 2 H, =CHN), 8.31 (br s, 2 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.8, 26.2, 51.2, 64.3, 64.8, 71.3, 76.2, 82.5, 94.0, 101.0, 122.2, 123.8, 128.8, 131.9, 132.0, 132.8, 144.3, 150.4, 161.4.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{56}H_{66}N_4O_{10}Si_2$ + Na: 1033.4215; found: 1033.4218.

Ethyl 6-*O*-(*tert*-Butyldimethylsilyl)-2,3,4-trideoxy-4-[2,4-dioxo-5-vinyl-3,4-dihydropyrimidin-1(2*H*)-yl]-α-D-*erythro*-hex-2-enopyranoside (10)

A solution of $Pd(Ph_3P)_2Cl_2$ (7.15 mg, 0.01 mmol) and compound **2** (101 mg, 0.2 mmol) in DMF (3 mL) was stirred at r.t. in a Schlenk tube under argon for 15 min. To this solution was added tributylvinyltin (0.12 mL, 0.4 mmol), and Et_3N (0.03 mL, 0.24 mmol), in DMF (1 mL), followed by the addition of 1,4-diethynylbenzene (18.9 mg, 0.15 mmol). After stirring for 5 h at 70 °C, the solution was filtered through Celite, and the solid was washed with EtOAc (2 × 5 mL). Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica gel (CH_2Cl_2–EtOAc, 7:3) to give compound **10** (70 mg, 86%) as a colorless solid; mp 54.5–56.5 °C; R_f = 0.65 (CH_2Cl_2–EtOAc, 7:3); $[\alpha]_D^{25}$ +63.3 (*c* = 1.0, CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $Si(CH_3)_2$], 0.83 (s, 9 H, *t*-C_4H_9), 1.24 (t, *J* = 7.1 Hz, 3 H, CH_3CH_2O), 3.57 (dq, *J* = 9.6, 7.1 Hz, 1 H, CH_3CH_2O), 3.67 (dd, *J* = 11.3, 5.6 Hz, 1 H, H-6), 3.70 (dd, *J* = 11.3, 4.3 Hz, 1 H, H-6), 3.81–3.92 (m, 2 H, CH_3CH_2O, H-5), 5.06 (br s, 1 H, H-1), 5.21 (br m, 1 H, H-4), 5.24 (dd, *J* = 11.4, 1.3 Hz, 1 H, =CH_2), 5.74 (dd, *J* = 10.1, 1.3 Hz, 1 H, H-3), 5.99 (dd, *J* = 17.5, 1.3 Hz, 1 H, = CH_2), 6.06 (ddd, *J* = 10.1, 2.6, 2.6 Hz, 1 H, H-2), 6.34 (dd, *J* = 17.5, 11.4 Hz, 1 H, =CH), 7.21 (s, 1 H, =CHN), 8.76 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = –5.1, –5.0, 15.6, 18.7, 26.2, 51.3, 64.1, 64.6, 71.3, 93.9, 113.6, 116.9, 127.8, 129.0, 131.3, 138.2, 150.9, 162.3.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{32}N_2O_5Si$ + Na: 431.1978; found: 431.1980.

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